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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 3	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 4	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 5	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 6	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 7	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 8	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 9	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 10	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 11	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 12	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 13	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 14	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 15	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 16	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 17	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 18	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS 19	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS 20	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS 21	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS 22	JUL 28	CA/CAplus patent coverage enhanced
NEWS 23	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 24	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 25	JUL 28	STN Viewer performance improved
NEWS 26	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced

Updated Search

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 NEWS 27  AUG 13  CA/CAplus enhanced with printed Chemical Abstracts
                  page images from 1967-1998
 NEWS 28  AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS 29  AUG 15  CAplus currency for Korean patents enhanced
 NEWS 30  AUG 25  CA/CAplus, CASREACT, and IFI and USPAT databases
                  enhanced for more flexible patent number searching

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE COVERS 1907 - 25 Aug 2008  VOL 149 ISS 9
FILE LAST UPDATED: 24 Aug 2008  (20080824/ED)

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 This file contains CAS Registry Numbers for easy and accurate
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=> s RNA () polymerase () protein?
        357529 RNA
         30121 RNAS
        363055 RNA
                 (RNA OR RNAS)
        226634 POLYMERASE
         10671 POLYMERASES
        228313 POLYMERASE
                 (POLYMERASE OR POLYMERASES)
       2610376 PROTEIN?
L1         229 RNA (W) POLYMERASE (W) PROTEIN?

=> s RdRp () protein?
           776 RDRP
           107 RDRPS
           788 RDRP
                 (RDRP OR RDRPS)
       2610376 PROTEIN?
L2          15 RDRP (W) PROTEIN?

=> s NS5B () protein?
          1040 NS5B
       2610376 PROTEIN?
L3         154 NS5B (W) PROTEIN?

=> s NSF () protein?
          3863 NSF
            20 NSFS
          3870 NSF
                 (NSF OR NSFS)
       2610376 PROTEIN?
L4          87 NSF (W) PROTEIN?

=> s l1 or l2 or l3 or l4
L5         482 L1 OR L2 OR L3 OR L4

=> s AtRdRP1 () protein?
             1 ATRDRP1
       2610376 PROTEIN?
L6           0 ATRDRP1 (W) PROTEIN?

=> s l5 () inhibitor?
       1117113 INHIBITOR?
L7           7 L5 (W) INHIBITOR?

=> s l7 and review/dt
       2176307 REVIEW/DT
L8           1 L7 AND REVIEW/DT

=> d l8, ibib abs hitstr, 1

L8   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2007:819460  HCAPLUS
```

DOCUMENT NUMBER: 149:94200
TITLE: A new method for HCV therapy: RNA-dependent RNA polymerase inhibitor
AUTHOR(S): Zhang, Xiu-jie; Han, Xiao-feng; Ouyang, Hong-sheng
CORPORATE SOURCE: College of Animal Husbandry and Veterinary Medicine, Jilin University, Changchun, 130062, Peop. Rep. China
SOURCE: Shengming De Huaxue (2007), 27(3), 251-253
CODEN: SDHUEE; ISSN: 1000-1336
PUBLISHER: Shengming De Huaxue Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review. Hepatitis C is caused by infection of hepatitis C virus (HCV), a worldwide spread RNA virus; about 50% HCV infected cases would developed into chronic hepatitis, which has become a great problem for human health. NS5B protein, a non-structural protein (NS protein) of HCV with the function of RNA-dependent RNA polymerase (RdRp), is the core substance in HCV replication. Therefore, NS5B inhibitors can interrupt HCV replication and may play as anti-HCV drugs. Much work has been done on NS5B inhibitor development and some NS5B inhibitors have enter the clin. trial. Progress of NS5B inhibitor studies are reviewed with 14 refs.

=> s l5 and antagonist?
264649 ANTAGONIST?
L9 3 L5 AND ANTAGONIST?

=> s l9 and review/dt
2176307 REVIEW/DT
L10 0 L9 AND REVIEW/DT

=> d 19, ibib abs hitstr, 1-3

L9 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1064219 HCAPLUS
DOCUMENT NUMBER: 147:383999
TITLE: Detection of gene expression by specific cell types in mixed samples or tissues such as mouse thymus cortex or medullary stromal cells using DGEM (differential gene expression mapping)
INVENTOR(S): Petrie, Howard T.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 257pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106507	A2	20070920	WO 2007-US6363	20070314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,

RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-782124P P 20060314

AB Differential gene expression mapping (DGEM) utilizes (1) laser capture microdissection or other methods of microdissection of the tissue regions of interest; (2) microarray screening of RNA isolated from the microdissected regions and anal. of purified individual cellular components from the tissue; and (3) computational profiling or subtraction to identify gene expression by specific cell types in situ. The method was applied to stromal cells from whole cortical and medullary regions of C57BL6 mouse thymus. As a result, DGEM, a reverse identification approach, solves previously insurmountable problems, as the lymphoid progenitors can be readily isolated, allowing fluctuations in receptor expression on lymphoid cells to be used to predict stratified stromal signals. An algorithmic approach can be used for calculating the expression profile of a tissue/sample of interest that consists of at least two types of cells. Specifically, the approach electronically subtracts the expression profile of one component of a sample from the expression profile of the total sample, thus revealing the profiles of the other component. To confirm the robustness of the DGEM procedure, the gene expression profiles from each sample of whole medulla, whole cortex, cortical thymocytes and medullary thymocytes was sorted based only on the expression data.

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:67469 HCAPLUS
DOCUMENT NUMBER: 142:309250
TITLE: Inhibition of native hepatitis C virus replicase by nucleotide and non-nucleoside inhibitors
AUTHOR(S): Ma, Han; Leveque, Vincent; De Witte, Anniek; Li, Weixing; Hendricks, Than; Clausen, Saundra M.; Cammack, Nick; Klumpp, Klaus
CORPORATE SOURCE: Roche Palo Alto LLC, Palo Alto, CA, 94304, USA
SOURCE: Virology (2005), 332(1), 8-15
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A number of nucleotide and non-nucleoside inhibitors of HCV polymerase are currently under investigation as potential antiviral agents to treat HCV-infected patients. HCV polymerase is part of a replicase complex including the polymerase subunit NS5B together with other viral and host proteins and viral RNA. The RNA synthesis activity of the native replicase complex was inhibited by 3'-deoxy-CTP, a chain-terminating nucleotide analog, but not inhibited by non-nucleoside NS5B polymerase inhibitors of three different structural classes. The HCV replicase was also resistant to heparin, a broad-spectrum, RNA-competitive polymerase inhibitor. Prebinding of the recombinant NS5B protein with a RNA template rendered the polymerase largely resistant to the inhibition by heparin and the non-nucleoside inhibitors, but did not affect the inhibitory potency of 3'-deoxy-CTP. Therefore, the HCV

replicase showed a similar pattern of inhibitor sensitivity as compared to RNA-bound NS5B. These results suggest that the native HCV replicase complex represents a stable and productive polymerase-RNA complex. The allosteric non-nucleoside NS5B polymerase inhibitors are inactive against established HCV replicase but may function antagonistically with the formation of a productive enzyme-template complex.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:893420 HCAPLUS
DOCUMENT NUMBER: 136:112840
TITLE: Binding of the β2 adrenergic receptor to N-ethylmaleimide-sensitive factor regulates receptor recycling
AUTHOR(S): Cong, Mei; Perry, Stephen J.; Hu, Liaoyuan A.; Hanson, Phyllis I.; Claing, Audrey; Lefkowitz, Robert J.
CORPORATE SOURCE: Howard Hughes Medical Institute, Departments of Medicine and Biochemistry, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Journal of Biological Chemistry (2001), 276(48), 45145-45152
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Following agonist stimulation, most G protein-coupled receptors become desensitized and are internalized, either to be degraded or recycled back to the cell surface. What dets. the fate of a specific receptor type after it is internalized is poorly understood. Here we show that the rapidly recycling β2 adrenergic receptor (β2AR) binds via a determinant including the last three amino acids in its carboxyl-terminal tail to the membrane fusion regulatory protein, N-ethylmaleimide-sensitive factor (NSF). This is documented by in vitro overlay assays and by cellular coimmunopptns. Receptors bearing mutations in any of the last three residues fail to interact with NSF. After stimulation with the agonist isoproterenol, a green fluorescent protein fusion of NSF colocalizes with the wild type β2AR but not with a tail-mutated β2AR. The β2AR-NSF interaction is required for efficient internalization of the receptors and for their recycling to the cell surface. Mutations in the β2AR tail that ablate NSF binding reduce the efficiency of receptor internalization upon agonist stimulation. Upon subsequent treatment of cells with the antagonist propranolol, wild type receptors return to the cell surface, while tail-mutated receptors remain sequestered. Thus, the direct binding of the β2AR to NSF demonstrates how, after internalization, the fate of a receptor is reliant on a specific interaction with a component of the cellular membrane-trafficking machinery.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 10:46:13 ON 25 AUG 2008)

Updated Search

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     FILE 'HCAPLUS' ENTERED AT 10:46:41 ON 25 AUG 2008
L1          229 S RNA () POLYMERASE () PROTEIN?
L2           15 S RDRP () PROTEIN?
L3          154 S NS5B () PROTEIN?
L4           87 S NSF () PROTEIN?
L5          482 S L1 OR L2 OR L3 OR L4
L6            0 S ATRDRP1 () PROTEIN?
L7            7 S L5 () INHIBITOR?
L8            1 S L7 AND REVIEW/DT
L9            3 S L5 AND ANTAGONIST?
L10           0 S L9 AND REVIEW/DT

=> s l5 and virus
        393280 VIRUS
         82854 VIRUSES
        408184 VIRUS
                (VIRUS OR VIRUSES)
L11        273 L5 AND VIRUS

=> s l11 and review/dt
       2176307 REVIEW/DT
L12          9 L11 AND REVIEW/DT

=> d his

     (FILE 'HOME' ENTERED AT 10:46:13 ON 25 AUG 2008)

     FILE 'HCAPLUS' ENTERED AT 10:46:41 ON 25 AUG 2008
L1          229 S RNA () POLYMERASE () PROTEIN?
L2           15 S RDRP () PROTEIN?
L3          154 S NS5B () PROTEIN?
L4           87 S NSF () PROTEIN?
L5          482 S L1 OR L2 OR L3 OR L4
L6            0 S ATRDRP1 () PROTEIN?
L7            7 S L5 () INHIBITOR?
L8            1 S L7 AND REVIEW/DT
L9            3 S L5 AND ANTAGONIST?
L10           0 S L9 AND REVIEW/DT
L11         273 S L5 AND VIRUS
L12           9 S L11 AND REVIEW/DT

=> s l12 not l9
L13           9 L12 NOT L9

=> d l13, ibib abs hitstr, 1-9

L13  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:146559  HCAPLUS
DOCUMENT NUMBER:          148:577886
TITLE:                    Protein expression system using Leishmania
AUTHOR(S):                Wu, Xiao-wen; Xu, Fan-hong; Zhu, Wei; Zhang, Guang-pu;
                          Guo, Sheng-qi
CORPORATE SOURCE:         First Research Office, Shanghai Institute of
                          Biological Products, Shanghai, 200052, Peop. Rep.
                          China
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SOURCE: Guoji Shengwu Zhipinxue Zazhi (2007), 30(4), 148-150
CODEN: GSZZAK; ISSN: 1673-4211
PUBLISHER: Guoji Shengwu Zhipinxue Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. This article reviews the protein expression system using Leishmania. The article discusses the gene expression from transcription by T7 RNA polymerase and RNA polymerase II. The article also discusses the expression of HBsAg antigen.

L13 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:819460 HCAPLUS
DOCUMENT NUMBER: 149:94200
TITLE: A new method for HCV therapy: RNA-dependent RNA polymerase inhibitor
AUTHOR(S): Zhang, Xiu-jie; Han, Xiao-feng; Ouyang, Hong-sheng
CORPORATE SOURCE: College of Animal Husbandry and Veterinary Medicine, Jilin University, Changchun, 130062, Peop. Rep. China
SOURCE: Shengming De Huaxue (2007), 27(3), 251-253
CODEN: SDHUEE; ISSN: 1000-1336
PUBLISHER: Shengming De Huaxue Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Hepatitis C is caused by infection of hepatitis C virus (HCV), a worldwide spread RNA virus; about 50% HCV infected cases would developed into chronic hepatitis, which has become a great problem for human health. NS5B protein, a non-structural protein (NS protein) of HCV with the function of RNA-dependent RNA polymerase (RdRp), is the core substance in HCV replication. Therefore, NS5B inhibitors can interrupt HCV replication and may play as anti-HCV drugs. Much work has been done on NS5B inhibitor development and some NS5B inhibitors have enter the clin. trial. Progress of NS5B inhibitor studies are reviewed with 14 refs.

L13 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:741280 HCAPLUS
DOCUMENT NUMBER: 145:329946
TITLE: Nonstructural protein 5B of hepatitis C virus
AUTHOR(S): Lee, Jong-Ho; Nam, In Young; Myung, Heejoon
CORPORATE SOURCE: Department of Bioscience and Biotechnology, Hankuk University of Foreign Studies, Yongin, 449-791, S. Korea
SOURCE: Molecules and Cells (2006), 21(3), 330-336
CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER: Korean Society for Molecular and Cellular Biology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Since its identification in 1989, hepatitis C virus was the subject of extensive research. The biol. of the virus and the development of antiviral drugs are closely related. The RNA polymerase activity of nonstructural protein 5B was first demonstrated in 1996. NS5B is believed to localize to the perinuclear region, forming a replicase complex with other viral proteins. It has a typical polymerase structure with thumb, palm, and finger domains encircling the active site. A de novo replication initiation mechanism was suggested. To date, many small mol. inhibitors are known including nucleoside analogs,

non-nucleoside analogs, and pyrophosphate mimics. NS5B interacts with other viral proteins such as core, NS3, 4A, 4B, and 5A. The helicase activity of NS3 seems necessary for RNA strand unwinding during replication, with other nonstructural proteins performing modulatory roles. Cellular proteins interacting with NS5B include VAMP-associated proteins, heIF4AII, hPLIC1, nucleolin, PRK2, α-actinin, and p68 helicase. The interactions of NS5B with these proteins might play roles in cellular trafficking, signal transduction, and RNA polymerization, as well as the regulation of replication/translation processes.

REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:475491 HCAPLUS
DOCUMENT NUMBER: 141:65664
TITLE: Transcription and replication of influenza virus genome
AUTHOR(S): Honda, Ayae; Ishihama, Akira
CORPORATE SOURCE: Mol. Biol. Div., Nippon inst. Biol. Sci., Japan
SOURCE: Tanpakushitsu Kakusan Koso (2004), 49(8), 1204-1211
CODEN: TAKKAJ; ISSN: 0039-9450
PUBLISHER: Kyoritsu Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on the genome structure of influenza virus, its peculiar transcription mechanism, function regulation by "cap effector", a functional map of the viral RNA polymerase, proteins involved in functional transformation of RNA polymerase, and mols. determining the host factors.

L13 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:255241 HCAPLUS
DOCUMENT NUMBER: 141:67932
TITLE: Effects of genotypic variations on hepatitis C virus nonstructural protein 5B structure and activity
AUTHOR(S): Hong, Zhi; Ferrari, Eric B.; Skelton, Angela; Wright-Minogue, Jacquelyn; Zhong, Weidong; Lesburg, Charles A.
CORPORATE SOURCE: Department of Antiviral Therapy, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA
SOURCE: Frontiers in Viral Hepatitis (2003), 109-121.
Editor(s): Schinazi, Raymond F.; Sommadossi, Jean-Pierre; Rice, Charles M. Elsevier: Amsterdam, Neth.
CODEN: 69FEJF; ISBN: 0-444-50986-0
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review. Nonstructural protein 5B (NS5B) of hepatitis C virus (HCV) possesses an RNA-dependent RNA polymerase (RdRp) activity responsible for viral genome replication. It presents an excellent target for antiviral development. Recent studies revealed that removal of the C-terminal hydrophobic domain improved the solubility of NS5B to a level suitable for enzymic characterization and structural determination This hydrophobic C-terminal tail is highly conserved among all six genotypes of

HCV, indicating an important functional and structural role, presumably as a membrane anchor for the assembly of a replication complex. Similar hydrophobic domains were also identified in related viruses such as pestiviruses and GB viruses. Removal of these hydrophobic domains had a universal impact on enzyme solubility and resulted in production of soluble polymerases from all six HCV genotypes, as well as from pestiviruses and GB viruses. Biochem. characterization demonstrated that the activity of RdRps from different HCV genotypes/subtypes varied and lacked a clear correlation either to the response to combination therapy or to the plasma viremia levels. Structure-based surface variability anal. further identified highly conserved regions in the active site and predicted asym. distribution of important functionality and critical structural elements essential for replication.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:509812 HCAPLUS

DOCUMENT NUMBER: 134:97543

TITLE: Biochemical and immunologic properties of the nonstructural proteins of the hepatitis C virus: Implications for development of antiviral agents and vaccines

AUTHOR(S): De Francesco, Raffaele; Neddermann, Petra; Tomei, Licia; Steinkuhler, Christian; Gallinari, Paola; Folgori, Antonella

CORPORATE SOURCE: Istituto di Richerche di Biologia, Molecolare, "P. Angeletti," Pomezia, Rome, Italy

SOURCE: Seminars in Liver Disease (2000), 20(1), 69-83
CODEN: SLDIEE; ISSN: 0272-8087

PUBLISHER: Thieme Medical Publishers, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 150 refs. Infection with the hepatitis C virus (HCV) is the major cause of non-A, non-B hepatitis worldwide. The viral genome, a pos.-sense, single-stranded, 9.6-kb long RNA mol., is translated into a single polyprotein of about 3,000 amino acids. The viral polyprotein is proteolytically processed to yield all the mature viral gene products. The genomic order of HCV has been determined to be C → E1 → E2 → p7 → NS2 → NS3 → NS4A → NS4B → NS5A → NS5B. C, E1, and E2 are the virion structural proteins. Whereas the function of p7 is currently unknown, NS2 to NS5B are thought to be the nonstructural proteins. Generation of the mature nonstructural proteins relies on the activity of viral proteinases. Cleavage at the NS2-NS3 junction is accomplished by a metal-dependent autocatalytic proteinase encoded within NS2 and the N-terminus of NS3. The remaining downstream cleavages are effected by a serine proteinase contained also within the N-terminal region of NS3. NS3, in addition, contains an RNA helicase domain at its C-terminus. NS3 forms a heterodimeric complex with NS4A. The latter is a membrane protein that acts as a cofactor of the proteinase. Although no function has yet been attributed to NS4B, NS5A has been recently suggested to be involved in mediating the resistance of the HCV to the action of interferon. Finally, the NS5B protein has been shown to be the viral RNA-dependent RNA polymerase. This article reviews the current

understanding of the structure and the function of the various HCV nonstructural proteins with particular emphasis on their potential as targets for the development of novel antiviral agents and vaccines.
REFERENCE COUNT: 150 THERE ARE 150 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:435447 HCAPLUS
DOCUMENT NUMBER: 127:146877
ORIGINAL REFERENCE NO.: 127:28297a,28300a
TITLE: The nonstructural proteins of the hepatitis C virus. Structure and functions
AUTHOR(S): Neddermann, Petra; Tomei, Licia; Steinkuhler, Christian; Gallinari, Paola; Tramontano, Anna; De Francesco, Raffaele
CORPORATE SOURCE: Istituto Ricerche Biologia Molecolare "P. Angeletti", Rome, I-00040, Italy
SOURCE: Biological Chemistry (1997), 378(6), 469-476
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: de Gruyter
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review is given with many refs. The hepatitis C virus is the major causative agent of nonA-nonB hepatitis worldwide. Although this virus cannot be cultivated in cell culture, several of its features were been elucidated. The viral genome is a single-stranded, 9.5kb long RNA mol. of pos. polarity. The viral genome is translated into a single polyprotein of about 3000 amino acids. The virally encoded polyprotein undergoes proteolytic processing by a combination of cellular and viral proteolytic enzymes in order to yield all the mature viral gene products. The gene order of HCV was C-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B. The mature structural proteins, C, E1 and E2 were shown to arise from the viral polyprotein via proteolytic processing by host signal peptidases. Conversely, generation of the mature nonstructural proteins relies on the activity of viral proteases. Thus, cleavage at the NS2/NS3 junction is accomplished by a metal-dependent autoprotease encoded within NS2 and the N-terminus of NS3. The remaining cleavages downstream from this site are effected by a Ser protease contained within the N-terminal region of NS3. Besides the protease domain, NS3 also contains an RNA helicase domain at its C-terminus. NS3 forms a heterodimeric complex with NS4A. The latter is a membrane protein that acted as a cofactor of the protease. Whereas the NS5B protein was the viral RNA-dependent RNA polymerase, no function has yet been attributed to NS4B and NS5A. The latter is a cytoplasmic phosphoprotein and appears to be involved in mediating the resistance of the hepatitis C virus to the action of interferon.

L13 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:29133 HCAPLUS
DOCUMENT NUMBER: 122:72750
ORIGINAL REFERENCE NO.: 122:13675a,13678a
TITLE: Structure, organization, and expression of hepatitis C virus genome
AUTHOR(S): Fuke, Isao; Manabe, Sadao; Okayama, Hiroto
CORPORATE SOURCE: Research Foundation Microbial Diseases Osaka

University, Kanonji, 768, Japan
SOURCE: Asian Medical Journal (1994), 37(5), 240-5
CODEN: ASMJAB; ISSN: 0004-461X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 11 refs. Hepatitis C virus (HCV) is the major causative agent of posttransfusion non-A, non-B hepatitis, which has long been a serious medical problem worldwide. Following the isolation part of the HCV genome by Choo et al., the entire genome of ten independent HCV strains has subsequently been cloned and their primary structures have been elucidated. Sequence anal. has suggested that HCV is related to both flaviviruses and pestiviruses. The authors recently constructed a recombinant vaccinia virus that carried the entire HCV polyprotein coding region under an appropriate promoter. After infection of Change liver cells with the recombinant virus, the entire HCV polyprotein was produced and processed into core, envelope, E2, NS1, and NS3 proteins, as well as unexpectedly small NS4, NS5a, and NS5b proteins due to further cleavage of NS5 and perhaps NS2. Mutation and coexpression of studies of NS3 indicated that production of the nonstructural proteins of HCV absolutely requires an NS3-encoded putative protease.

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ACCESSION NUMBER: 1994:647238 HCAPLUS
DOCUMENT NUMBER: 121:247238
ORIGINAL REFERENCE NO.: 121:44959a,44962a
TITLE: DNA replication in filamentous bacteriophage
AUTHOR(S): Higashitani, Atsushi; Higashitani, Nahoko; Horiuchi, Kensuke
CORPORATE SOURCE: Dep. Microb. Genet., Natl. Inst. Genet., Mishima, 411, Japan
SOURCE: Tanpakushitsu Kakusan Koso (1994), 39(13), 2189-97
CODEN: TAKKAJ; ISSN: 0039-9450
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 19 refs. Nucleotide sequence of primer RNA, interactions between minus chain origin and DNA and RNA polymerase, protein binding to DNA, etc. were related to mechanisms of initiation of replication of minus and plus DNA chains of filamentous bacteriophage.